

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (previously presented) A method for treating or preventing pathophysiological consequences of mitochondrial respiratory chain dysfunction in a mammal comprising administering to said mammal in need of such treatment or prevention an effective amount of a pyrimidine nucleotide precursor.

2. (original) A method as in claim 1 wherein said respiratory chain dysfunction is caused by a mutation, deletion, or rearrangement of mitochondrial DNA.

3. (original) A method as in claim 1 wherein said respiratory chain dysfunction is caused by defective nuclear-encoded protein components of the mitochondrial respiratory chain.

4. (original) A method as in claim 1 wherein said respiratory chain dysfunction is caused by aging.

5. (original) A method as in claim 1 wherein said respiratory chain dysfunction is caused by administration of cytotoxic cancer chemotherapy agents to said mammal.

6. (original) A method as in claim 1 wherein said respiratory chain dysfunction

is a deficit in mitochondrial Complex I activity.

7. (original) A method as in claim 1 wherein said respiratory chain dysfunction is a deficit in mitochondrial Complex II activity.

8. (original) A method as in claim 1 wherein said respiratory chain dysfunction is a deficit in mitochondrial Complex III activity.

9. (original) A method as in claim 1 wherein said respiratory chain dysfunction is a deficit in mitochondrial Complex IV activity.

10. (original) A method as in claim 1 wherein said respiratory chain dysfunction is a deficit in mitochondrial Complex V activity.

11. (original) A method as in claim 1 wherein said pyrimidine nucleotide precursor is selected from the group consisting of uridine, cytidine, an acyl derivative of uridine, an acyl derivative of cytidine, orotic acid, an alcohol ester of orotic acid, or a pharmaceutically acceptable salt thereof.

12. (original) A method as in claim 11 wherein said pyrimidine nucleotide precursor is an acyl derivative of cytidine.

13. (original) A method as in claim 11 wherein said pyrimidine nucleotide

precursor is an acyl derivative of uridine.

14. (original) A method as in claim 11 wherein said acyl derivative of uridine is 2',3',5'-tri-O-acetyluridine.

15. (original) A method as in claim 11 wherein said acyl derivative of uridine is 2',3',5'-tri-O-pyruvyluridine.

16-17. (cancelled)

18. (original) A method as in claim 11 wherein said pyrimidine nucleotide precursor is administered orally.

19. (original) A method as in claim 11 wherein said pyrimidine nucleotide precursor is administered in a dose of 10 to 1000 milligrams per kilogram of bodyweight per day.

20. (original) A method as in claim 11 wherein said pyrimidine nucleotide precursor is administered in a dose of 100 to 300 milligrams per kilogram of bodyweight per day.

21. (original) A method as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is a congenital

mitochondrial disease.

22. (previously presented) A method as in claim 21 wherein said congenital mitochondrial disease is selected from the group consisting of Mitochondrial Encephalomyopathy, Lactic Acidemia, and stroke like episodes; Lerber's Hereditary Optic Neuropathy; Myclonic Epilepsy and "Ragged Red" (muscle) Fibers; Mitochondrial neurogastrointestinal encephalomyopathy; Neurogenic muscle weakness, Ataxia and Retinitis Pigmentosa; Progressive External Ophthalmoplegia; Leigh's Disease; and Kearns-Sayres Syndrome.

23. (original) A method as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is a neurodegenerative disease.

24. (original) A method as in claim 23 wherein said neurodegenerative disorder is Alzheimer's Disease.

25. (original) A method as in claim 23 wherein said neurodegenerative disorder is Parkinson's disease.

26. (original) A method as in claim 23 wherein said neurodegenerative disorder is Huntington's Disease.

27. (original) A method as in claim 23 wherein said neurodegenerative disorder is age-related decline in cognitive function.

28. (original) A method as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is a neuromuscular degenerative disease.

29. (original) A method as in claim 28 wherein said neuromuscular degenerative disease is selected from the group consisting of muscular dystrophy, myotonic dystrophy, chronic fatigue syndrome, and Friedreich's Ataxia.

30. (original) A method as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is developmental delay in cognitive, motor, language, executive function, or social skills.

31. (original) A method as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is selected from the group consisting of epilepsy, peripheral -neuropathy, optic neuropathy, autonomic neuropathy, neurogenic bowel dysfunction, sensorineural deafness, neurogenic bladder dysfunction, migraine, and ataxia.

32. (original) A method as in claim 1 wherein said pathophysiological consequence of mitochondrial respiratory chain dysfunction is selected from the group

consisting of renal tubular acidosis, dilating cardiomyopathy, steatohepatitis, hepatic failure, and lactic acidemia.

33. (original) A method for preventing death or functional decline of post-mitotic cells in a mammal due to mitochondrial respiratory chain dysfunction comprising administration of an effective amount of a pyrimidine nucleotide precursor.

34. (original) A method as in claim 33 wherein said post-mitotic cells are neurons.

35. (original) A method as in claim 33 wherein said post-mitotic cells are skeletal muscle cells.

36. (original) A method as in claim 33 wherein said post-mitotic cells are cardiomyocytes.

37. (original) A method for treating developmental delay in cognitive, motor, language, executive function, or social skills in a mammal comprising administration of an effective amount of a pyrimidine nucleotide.

38. (previously presented) A method as in claim 37 wherein said developmental delay is pervasive developmental delay or pervasive developmental delay – not otherwise specified.

39. (original) A method as in claim 37 wherein said developmental delay is Attention Deficit/Hyperactivity Disorder.

40. (original) A method as in claim 37 wherein said developmental delay is Rett's Syndrome.

41. (original) A method as in claim 37 wherein said developmental delay is autism.

42-46. (cancelled)

47. (original) A method as in Claim 1 further comprising administering pyruvic acid, a pharmaceutically acceptable salt thereof, or a pyruvic acid ester.

48. (original) A method as in claim 1 further comprising administering to the mammal an amount of creatine such that the combined amount of creatine and the pyrimidine nucleotide is effective to treat said consequences of mitochondrial respiratory chain dysfunction.

49. (original) A method as in claim 48 wherein said pyrimidine nucleotide is 2',3',5'-tri-O-acetyluridine.

von BORSTEL et al
Appl. No. 09/930,494
May 4, 2005

50. (cancelled)